Research Paper

Volume : 3 | Issue : 10 | October 2014 • ISSN No 2277 - 8179

A Comparison of the Efficacy and Tolerability of Antibiotics in the Treatment of Acute Rhinosinusitis in Adults

Medical Science

KEYWORDS : Acute bacterial sinusitis, Antibiotic, Amoxicillin-Clavulanate, Cefuroxime, Moxifloxacin

*** Dr.Anil.H.T** — Associate Professor, Department of ENT, Kempegowda Institute of Medical Sciences, K.R.Road, V.V Puram, Bangalore-560004. * Corresponding author

Dr.Amrita Suzanne Mathew — Post Graduate, Department of ENT, Kempegowda Institute of Medical Sciences, K.R.Road, V.V Puram, Bangalore-560004. Karnataka.

ABSTRACT

Objectives-to compare the efficacy and tolerability of amoxicillin-clavulanate, cefuroxime axetil and moxifloxacin in the treatment of acute bacterial rhinosinusitis in adults.

Methods-90 adults aged 18-40years, clinically diagnosed with acute rhinosinusitis,symptomatic for 7-28days, were randomised into three groups,each receiving an oral antibiotic ie.Amoxicillin-clavulanate(GroupA),Cefuroxime (GroupB),Moxifloxacin(GroupC) and evaluated on days 0,7,14,21,28,60 using Major Symptom Score,Visual Analogue Scale for quality of life and Axelsson's sinus X-ray score.Time to improvement, relapse,recurrence and adverse events were noted.

Result-In Group A,B,C clinical cure rate was 89.86%, 92.76%, 96.57% respectively; mean time to improvement was 4.36, 4.07, 3.39 days respectively. Relapse,recurrence and adverse events(diarrhoea, nausea and rash) were highest with amoxicillin-clavulanate.

Conclusion- Moxifloxacin shows highest efficacy and tolerability.Cefuroxime and amoxicillin-clavulanate have similar clinical cure rates. Cefuroxime has lower relapse,recurrence and adverse event rates.

INTRODUCTION

Sinusitis is defined as symptomatic inflammation of the paranasal sinuses (PNS).Since sinusitis almost always involves the nasal cavity, the term rhinosinusitis is preferred[1]. Sinusitis is a leading healthcare problem believed to be increasing in both incidence and prevalence[2].

Sinusitis generally develops as a complication of bacterial,viral or allergic inflammation of the upper respiratory tract.Numerous bacterial pathogens are involved in acute sinusitis.The direct and indirect virulent characteristics of these bacteria require the administration of appropriate antimicrobial therapy directed against all pathogens in mixed infections[3].

According to various sources,the cost of this disease appears to be staggering[2]. Antibiotics reduce the incidence of clinical failures by one half compared to no treatment,and when coupled with clinical criteria based diagnosis,present the most cost effective treatment strategy[4].

Antimicrobials that are most effective in the management of acute bacterial sinusitis(ABRS) are amoxicillin-clavulanate,newer quinolones (moxifloxacin)and second generation cephalosporins(cefuroxime,cefpodoxime, cefprozil or cefdinir)[3].However there is little information to allow doctors to determine the best initial choice of antibiotic[5].

Thus this study was undertaken with the aim of comparing the efficacy and tolerability of amoxicillin-clavulanate, cefuroxime axetil and moxifloxacin in the treatment of adults with acute rhinosinusitis(ARS).

MATERIALS AND METHODS

A randomised study was conducted from November 2013 to July 2014 at the outpatient department of the Department of ENT,Kempegowda Institute of Medical Sciences, Bangalore.

90 adults of both sexes aged 18-40years, clinically diagnosed with ARS with signs and symptoms for >7days but <28days, confirmed by nasal endoscopy, with/without history of previous sinus surgery,were included in the study.

Those with history of chronic sinusitis (>four weeks of continuous symptoms), allergic rhinitis,anatomical/functional abnormality of nose/PNS,bacteremia/ meningitis/infection infiltrating neighbouring tissues,immunodeficiency diseases,received systemic antibacterial therapy likely to be effective in the treatment of ABRS for >24hours within 5-6days of enrolment,requirement for concomitant systemic antibacterial therapy with agents other than those in this study,currently receiving topical nasal corticosteroids(unless they have been on a stable dose for >4weeks before enrolment),requirement for concomitant therapy with systemic corticosteroids, pregnant/breast feeding, received an investigational drug in the past 30days, unable to take oral medication,history of allergy to drugs being used in the study/related compounds,other systemic illness,attrition to follow up or death from a cause not related to the study parameters in the observation period, were excluded from the study.

A clinical diagnosis of ARS was made based on the presence of atleast two major or one major and two minor symptoms as follows:

Major criteria–purulent anterior nasal discharge, purulent/discoloured posterior nasal discharge,nasal congestion/ obstruction, facial congestion/ fullness, facial pain/pressure,hyposmia/ anosmia, fever.

Minor criteria– headache, earache/ pressure/fullness, halitosis, dental pain, cough, fatigue.

Diagnosis was confirmed by nasal endoscopy.90 patients who met the inclusion criteria were randomised into three groups of 30 each.Group A received oral Amoxicillin-clavulanate 625mg b.i.d for 10days,Group B received oral Cefuroxime axetil 500mg b.i.d for 10days and Group C received oral Moxifloxacin 400mg o.d for 7days.Concomitant analgesic,antihistamine,decongestant was prescribed. Day of recruitment and initiation of antibiotic was considered as day 0. Follow up was conducted on days 7,14,21,28 and 60.

The Major Symptom Score(MSS) was calculated as a sum of the following scores on each visit:

A) Facial pain,pressure,tenderness on palpation over PNS

0=None
1=Mild-Easily tolerated
2=Moderate-Bothersome but tolerable
3=Severe-Hard to tolerate;interferes with activities of daily living(ADL) and/or sleeping

B) Sinus headache(forehead,eye-region,temple)

0 = None
1 = Mild-Allowing normal activity
2 = Moderate-Disturbing but not prohibiting normal activity,bed rest not necessary
3 = Severe-Normal activity discontinued, bed rest necessary

C) Rhinorrhoea(nasal discharge/runny nose)

0=None
1= Mild-Snuffles;occasional wiping and/or nose blowing
2= Moderate-Frequent wiping and/or nose blowing;frequently interrupts talking
3= Severe-Very frequent wiping and/or nose blowing;interferes with ADL and/or sleeping

D) Post-nasal drip(mucous in the throat)

0=None
1= Mild-Occasional throat clearing
2= Moderate-Frequent throat clearing; frequently interrupts talking
3= Severe-Very frequent throat clearing;constantly interrupts talking; interferes with ADL and/or sleeping

E) Nasal congestion/stuffiness

0=None
1= Mild-Slight block in one/both nostrils; nasal air flow somewhat impeded; no/infrequent mouth breathing
2= Moderate-Moderate block in one/both nostrils;nasal air flow noticeably impaired; frequent mouth breathing
3= Severe-Both nostrils completely blocked;mouth breathing all/almost all of the time.

Quality of life(QoL) was assessed by the 0-100 point Visual Analogue Scale(VAS) each visit.

X-ray of the PNS(Water's view) was taken on days 0 and 28, and Axelsson's scoring applied:

1=Mucous membrane thickening <6mm
2=Mucous membrane thickening >6mm
2=Air-fluid level
3=Mucous membrane thickening <6mm+air-fluid level
4=Mucous membrane thickening >6mm+air-fluid level
6=Complete sinus opacity

Primary outcome measure was clinical cure.Secondary outcome measures were time to improvement(number of days between initial visit and subjective improvement),relapse(subjective lack of improvement on days21 and 28 in a patient who had improved on day14) and recurrence(symptoms lasting >10days during the second month of follow up in a patient who had improved on day28).Adverse events,if any,were recorded.

RESULTS

The mean age of the study patients(57 males and 33 females)was 28.7±2.54years, with a range of 18-40years.

There was no significant difference in baseline medical history,signs and symptoms or radiographic scoring between groups on the first visit.Following administration of medication,significant reduction in MSS and improvement in QoL was seen from day7 onwards in all groups.(Table 1)

Radiographic scoring showed improvement by decrease in mean Axelsson's score(day1,28) in 56% of patients in group A(4.43,2.36), 57% in group B(4.5,1.97) and 60% in group C(4.39,1.20).

Mean time to improvement in Group A,B,C was 4.36,4.07,3.39 days respectively.Clinical cure rate was higher in the moxifloxacin group,while relapse,recurrence and adverse events (diarrhoea, nausea,rash)were most common in the amoxicillin-clavulanate group.(Graph 1).

DISCUSSION

Acute bacterial sinusitis usually occurs following an upper respiratory infection that results in obstruction of the osteomeatal complex,impaired mucociliary clearance and overproduction of secretions[6].

Our study included adults aged <40years as older subjects demonstrate significantly lower ciliary beat frequency,thus explaining the occurrence of frequent respiratory tract infection above this age[7].

The common bacterial pathogens in acute sinusitis are Streptococcus pneumoniae, Haemophilus influenzae,Moraxella catarrhalis and Staphylococcus aureus[3]. S.pneumoniae and H.influenzae account for >70% of cases of community acquired ABRS in adults[6].

Bacterial and viral sinusitis are difficult to differentiate on clinical grounds.The clinical diagnosis of ABRS should be reserved for patients with symptoms lasting ≥7days.Patients with symptoms lasting <7days are unlikely to have bacterial infection[8]. Therefore patients with symptoms of sinusitis for the past 7-28 days were included in our study.

Sinus radiographic studies may help differentiate a common cold from ABRS.A normal sinus Xray has a negative predictive value of 90-100% particularly for frontal and maxillary sinuses[6]. The positive predictive value of X-rays using opacification and air-fluid levels as end points is 80-100%, but the sensitivity is low since only 60% of patients with acute sinusitis show these changes[6],as was similarly observed in our study.

Rapid emergence of antibiotic resistant organisms associated with ABRS has made choosing an antibiotic more difficult.Studies have shown an increasing emergence of antibiotic resistant S.pneumoniae and H.influenzae due to beta-lactamase production.Resistance to macrolides,doxycycline and trimethoprim-sulphamethoxazole is common. Amoxicillin-clavulanate and fluoroquinolones currently have the best coverage for H.influenzae and S.pneumoniae.Sinus puncture studies have shown eradicated pathogens in atleast 95% of patients after a course of antibiotics[9].

Complications of untreated sinusitis can be serious,including brain abscess,orbital cellulitis,subdural empyema and meningitis.A study by Ferranti et.al. showed that treatment of ABRS with any antibiotic reduced the rate of clinical failures by half[5].In a study by Richard et.al.,it was seen that antimicrobials increase cure rate in patients with ABRS by 15% at 7-12 days when compared with a placebo[10].

Studies have revealed a similar success rate(>85%) between amoxicillin-clavulanate and cefuroxime in the treatment of ABRS[9],which concurred with our study results.

Our study showed similar clinical response between amoxicillin-clavulanate and cefuroxime,but the former had higher relapse,recurrence and adverse event rates.Namyslowski et.al compared the efficacy and tolerability of amoxicillin-clavulanate with cefuroxime axetil in the treatment of adults with ABRS,concluding that both drugs have similar response and cure rates,but cefuroxime had a higher clinical relapse rate[11].Camacho et.al compared amoxicillin-clavulanate and cefuroxime in the treatment of ABRS and showed that both had similar cure rates but amoxicillin-clavulanate had a higher incidence of drug related adverse events particularly diarrhoea[12],as was seen in our study.

Volume : 3 | Issue : 10 | October 2014 • ISSN No 2277 - 8179

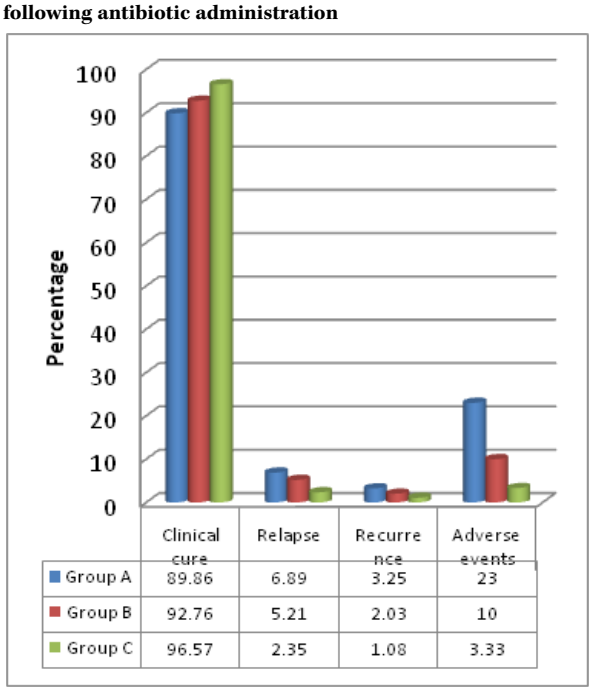
The use of fluoroquinolones for ABRS is relatively new9.Results similar to those in our study were seen in a trial by Siegert et.al. which showed that adults with ABRS treated with moxifloxacin had a higher clinical success rate,higher bacteriological success rate and fewer serious adverse events than those treated with cefuroxime axetil[13].

CONCLUSION

Moxifloxacin was the most efficacious antibiotic,with the highest clinical cure rate,lowest relapse and recurrence rate,and was best tolerated due to once daily dosing and lowest adverse event rate.Cefuroxime axetil and Amoxicillin-clavulanate have similar clinical response rates,however Cefuroxime showed lower rates of relapse, recurrence and adverse events.

Day	Mean Major Symptom Score			Mean VAS score for QoL		
	Group A	Group B	Group C	Group A	Group B	Group C
0	55.86	54.93	56.02	13.24	13.41	13.82
7	29.54	27.91	21.82	10.91	9.60	8.05
14	13.68	10.81	8.95	5.11	3.86	2.10
21	6.28	3.93	1.85	2.92	1.99	0.92
28	8.35	2.88	1.56	2.99	1.85	0.89
60	8.72	2.59	1.52	3.05	1.73	0.82

(Table 1). – Comparison of MSS and QoL between groups following antibiotic administration



(Graph 1). – Comparison of clinical outcome following antibiotic administration

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